A Novel LC-MS/MS Assay for Quantifying Dermatan Sulfate as a Cerebrospinal Fluid Biomarker for Mucopolysaccharidosis II Disease

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METHODS

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The ratio of the measured DS4S/6S concentration to the nominal concentration of DS was calculated. It is used as a correction factor to convert DS concentration to normalized DS4S concentration.

DS was used to establish the standard curve and make the QC samples to eliminate the variation from the enzymatic digestion.

QC samples are prepared in authentic CSF, except LQC samples are prepared in artificial CSF (aCSF), due to endogenous nature of DS.

RESULTS

Method Validation

Method Validation (continued)

Parallelism

Three different lots of authentic human CSF were analyzed by using standard addition (authentic CSF curve) and a surrogate matrix curve (aCSF curve). The endogenous DS levels measured by two curves are similar, and the slopes of calibration curves are also very similar, confirming the excellent surrogacy of the aCSF.

Sample Analysis

Analysis of DS in normal individuals and MPS II patients

The concentrations of DS in CSF from 50 normal individuals and 21 untreated MPS II patients were tested utilizing the described method. The results showed markedly increased concentration of CSF DS (11-fold) in MPS II patients, compared with normal subjects (t test; p < 0.0001).

CONCLUSIONS

An LC-MS/MS method for DS quantitation in human CSF has been developed and validated following FDA guidelines.

This method was successfully applied to analyze DS in normal individuals and MPS II patients. A significant increase in DS levels was observed in patients with MPS II compared with normal controls.

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